REMARKS

Status of the Claims

All claim cancelations, withdrawals, and amendments are made without prejudice or disclaimer to the right to pursue canceled, non-elected, or omitted subject matter in one or more continuation or divisional applications.

By virtue of the Listing of Claims presented herein, claims 1-3, 5-12, and 14-32 are pending.

Claims 7 and 15-21 were withdrawn in a previous response, without prejudice or disclaimer, as directed to non-elected subject matter.

Claim 1 has been herein amended as follows: to recite that the claim recites a method for treating, alleviating, or preventing an intestinal damage; that the said intestinal damage recited in the claim comprises a morphological damage; and that the recited active fragment of PYY comprises amino acids 22-28 of the amino acid sequence set out in SEQ ID NO:2. Basis for the amendment is found at, for example at: paragraph [0023], which discloses that "administration of an effective amount of PYY or agonist thereof protects the intestinal mucosa distal to the stomach. In another embodiment of the present invention, peripheral administration of an effective amount of PYY or agonists thereof reduces intestinal damage in the colon, including, for example, intestinal damage to the colon associated with inflammatory bowel disease; paragraphs [0054] through [0065], which disclose that administration of PYY or PYY agonists reduce and/or protect from intestinal damage; and [0029], [0030], and [0066] which collectively disclose that "[b]y 'PYY agonist' is meant any compound which elicits an effect of PYY to protects [sic] from or reduce colon injury associated with inflammatory bowel disease as exemplified in Example 1…and which binds specifically in a Y receptor assay (Example 4) or in a competitive binding assay with labeled PYY or PYY(3-36) from certain tissues having an abundance of Y receptors [see, e.g., paragraph [0029])…Such agonists can comprise a polypeptide having…an active fragment of PYY (see, e.g., paragraph [0030])." With respect to "PYY" as recited in the claim, Applicant notes that "PYY" is identified in the subject specification as SEQ ID NO:2.

With respect to basis for the recitation, "wherein said active fragment comprises amino acids 22-28 of the amino acid sequence set out in SEQ ID NO:2", Applicant notes that such

active fragment consisting of amino acids 22-28, as well as multiple such active fragments comprising amino acids 22-28, which were available at the tine of the priority filing date of the subject application are disclosed in the following documents, for example, all of which are of record in the subject case: Balasubrumaniam et al., *Peptide Research* (1988) at, e.g., Figure 2, Table 2, and column 1 of page 34; US 5,604,203 (1997) at, e.g., Tables 1, 2, 3, and 4 and Figures 2 and 4; WO 03/026591 (2003) at, e.g., Table 1, Table 2, and page 49, line 17, through page 77, line 6. In this regard, Applicant notes that "information incorporated is as much a part of the application as filed as if the text was repeated in the application, and should be treated as part of the text of the application as filed. MPEP 2163.07(b). Further, "there is no *per se* rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of **known** structure." *Falkner* at 1366 (emphasis added). Furthermore, "[n]one of the cases to which the Board attributes the requirement of total DNA re-analysis, *i.e.*, *Regents v. Lilly, Fiers v. Revel, Amgen*, or *Enzo Biochem*, require a re-description of what was already known." *Capon v. Eshhar*, 76 USPQ2d 1078 (Fed. Cir. 2005).

New Claims 22 through 32 have been added. Claims 22 through 29 find basis, e.g., at page 7, paragraph [0066], which discloses, for example, that exemplary PYY fragments which may be employed as PYY agonists in the claimed methods include each of the fragments as recited in Claims 22-29. Claims 30-32 find basis, e.g., in the EXAMPLES section, beginning at the first line of page 6. In particular, paragraphs [0050] through [0064], including TAPLE 1, which discloses the reduction, amelioration, and/or prevention of the recited morphological damage resultant from bowel injury, when such PYY agonists are administered in accordance with the claimed methods.

No new matter has been introduced by virtue of the amendments to the claims as reflected above.

Withdrawn Objections and/or Rejections

Applicants acknowledge the Examiner's withdrawal of the previous objection to Claim 1 for the

minor informality that was corrected in Applicant's response filed December 17, 2007.

Claim Rejections

Applicants have carefully considered the points raised in the outstanding Office Action and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

Rejection under 35 U.S.C. § 112, first paragraph: written description

Claims 1-3, 5, 6, and 8-12 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, in response to Applicant's presentation of numerous references demonstrating numerous active PYY analogs, which comprise PYY active fragments as recited in Applicant's claims, the Examiner alleges "[t]he cited references do not teach *the* structural determinant, "an active fragment of PYY". If Applicants believe that the prior art teaches representative species of the genus of agonists in the context of the claimed methods, they are requested to clearly point them out; if Applicants believe that the prior art teaches *the* structural feature of the encompassed genus of PYY agonist or the active fragment of PYY, they are also requested to clearly state what *it* is and where *it* is taught."(italics in quotations added.) Applicant traverses the rejection.

First, Applicant notes that the Examiner's invitation to "clearly state" what "*the* structural feature of the encompassed genus of PYY agonist or *the* active fragment of PYY" is and "where *it* is taught", implies that there must necessarily exist only one sole such "structural feature" that must be possessed by a PYY fragment in order for that fragment to constitute "an active fragment". The Examiner has provided no evidentiary basis to support this implied assertion. Indeed, the references cited by Applicant and of record in the subject case suggest the contrary, insofar as a variety of "structural determinants" are disclosed by virtue of the multiple "active fragments of PYY", which fragments correspond to different region and different analogs of native full-length PYY (see, e.g., WO 03/026591, Table 1, Table 2, and page 49, line 17, through page 77, line 6). Thus, not only does the Examiner beg the question that there exists a single,

invariant, "structural determinant" that must be possessed by a peptide in order to such peptide to constitute an "an active fragment of PYY" --the art at the art at the time refutes such a notion insofar as the art recognized that, in fact, such a peptide may possess one or more of a variety of "structural determinants" and constitute "an active fragment of PYY" as that term is understood and employed in the subject application and claims. The Examiner has provided no evidence in the art to contradict this.

Secondly, Applicant notes that the recitation, "structural determinant" does not appear in the claims; what does appear in the claims is the recitation "active fragment of PYY"; and as described above and in previous response(s), a variety of multiple such "active fragments of PYY", many of which necessarily comprise multiple and/or differing structural determinants, were available in that art at the time of priority date of the subject application:

> Additionally, Applicants note that Blundell et al. (1981) (submitted herewith) described the structure of the canonical PP fold, to atomic resolution, and identified secondary structural characteristics of the PP fold motif, including regions containing α-helical and β-sheet character, as well as specific residues and residue contacts involved in maintenance of PP fold integrity. Whereas the presence of the PP fold motif has been attributed to all members of the PP/NPY/PYY family of peptides (see, e.g., Keire et al., *Peptides*, pp. 314 (February 2002) (of record)) and particularly relevant for PYY structural integrity and activity (see, e.g., Keire et al., *Biochemistry* (2000) (of record)), additional structural determinants unique to numerous PYY and PYY analogs, and correlations of such determinants to PYY and PYY agonist function, were subsequently disclosed in the art (see, e.g., Keire et al., *Peptides*, (2002) (of record); Keire et al., *Am J. Physiol. Gastointest. Liver. Physiol* .(2000) (of record); U.S. Patent 5, 604,203 (of record); WO 03/026591 (of record); Bard *et al., J. Biol. Chem.* (1995) (submitted herewith); and Gehlert *et al.*, *Peptides* (1995) (submitted herewith)). Thus, numerous exemplary PYY and PYY agonists, their structures, and their associated receptor affinities, receptor selectivities, and exemplary biological activities (Applicant's Response mailed December 19, 2007; paragraph bridging pages 7 and 8).

Accordingly, the Examiner's request for Applicant to "clearly state what ['the structural determinant'] is and where ['the structural determinant'] is" is misplaced and inappropriate.

Nonetheless, and without acquiescing to the propriety of the Examiner's requirement, Applicant has amended the claims to recite that the recited "active fragment of PYY" comprises amino acids 22-28 of SEQ ID NO: 2. Applicant notes that this amino acid sequence (e.g., amino acids 22-28 of PYY) is demonstrated, for example, in Balasubrumaniam et al., *Peptide Research* (1988) at, e.g., Figure 2, Table 2, and column 1 of page 34 to comprise a "structural determinant" that is sufficient to generate "an active fragment of PYY". In this regard, Applicant notes that, as explained in Applicant's previous response, "there is no *per se* rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of **known** structure." *Falkner* at 1366 (emphasis added). Furthermore, "[n]one of the cases to which the Board attributes the requirement of total DNA re-analysis, *i.e.*, *Regents v. Lilly, Fiers v. Revel, Amgen*, or *Enzo Biochem*, require a re-description of what was already known." *Capon v. Eshhar*, 76 USPQ2d 1078 (Fed. Cir. 2005). Accordingly, Applicant submits that the requirements of Section 112 are satisfied with respect to the instant claims.

With respect to the Examiner's requirement to "clearly point [representative species of the genus of active fragments of PYY] out", Applicant notes that, as mentioned above, the Examiner was directed to disclosures of exemplary such representative active fragments of PYY. Nonetheless, Applicant submits that exemplary such species are clearly pointed out, for example, in: WO 03/026591, Table 1, Table 2, and page 49, line 17, through page 77, line 6; U.S. Patent 5, 604,203 throughout: Tables 1, 2, and 3, columns 9 and 10, Figures 2, 3,and 4, in particular; Balasubramaniam et al, *Peptide Research* (1988) throughout: Figure 2, Table 2, and column 1 of page 34, in particular. Again, in this regard, Applicant notes that, as explained in Applicant's previous response, "there is no *per se* rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of **known** structure." *Falkner* at 1366 (emphasis added). Furthermore, "[n]one of the cases to which the Board attributes the requirement of total DNA re-analysis, *i.e.*, *Regents v. Lilly, Fiers v. Revel, Amgen*, or *Enzo Biochem*, require a re-description of what was already known." *Capon v. Eshhar*, 76 USPQ2d 1078 (Fed. Cir. 2005). Accordingly, Applicant submits that the requirements of Section 112 are satisfied with respect to the instant claims.

Contrary to the Examiner's assertions, the genus of active fragments of PYY, as recited in the claims, is adequately described in the instant application in the context to that which was

known in the art at the time of the priority date of the subject application. The Section 112 rejection is in error and should be withdrawn.

Rejection under 35 U.S.C. § 102(b)

Claims 1, 2, 5, and 10-12 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Balasubramaniam (U.S. Patent No. 5, 604, 203), hereinafter '203. Specifically, the Examiner repeats the assertion that "Balasubramaniam teaches treating any gastrointestinal disorders that are associated with excess electrolyte and water secretion as well as decreased absorption, such as infectious diarrhea resulting from surgery (column 16)… Balasubramaniam further teaches that PYY plays a physiological role in regulating intestinal secretion and absorption, serving as natural inhibitors of diarrhea (column 1, lines 35-54; column 6, lines 43-67. Thus, Balasubramaniam teaches administering PYY to a subject to treat intestinal damages associated with these diseases." (Office Action mailed March 5, 2008, page 6, lines 4-17). Applicant traverses.

Again, the Examiner's characterization of the alleged teachings of the reference simply provides no nexus between the alleges treatment of the recited disorders and treating ameliorating, preventing, or protecting from intestinal damage that is inflicted on a subject as a result of experiencing such disorders. Additionally, the Examiner again failed to provide any evidence elsewhere in the art that would teach such a nexus. Accordingly, because the cited reference does not teach, explicitly or inherently, that intestinal damage inflicted as a result of experiencing such disorders is necessarily and unequivocally ameliorated, prevented, or protected from by practicing the alleged prior art method, the reference does not anticipate the claims:

To anticipate a claim, a reference must disclose every element of the claim. *Verdegaal Bros. v. Union Co. of California*, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987) and In re Donohue, 766 F.2d 531, 534, 226 U.S.P.Q. 619, 621 (Fed. Cir. 1985). An anticipation rejection requires a showing that each element of the claim is found in a single reference, practice or device. In re Donohue, 766 F.2d 531, 534, 226 U.S.P.Q. 619, 621 (Fed. Cir. 1985). The absence of a single claimed element from a cited reference precludes a finding of anticipation. Atlas Powder Company v. E.I. du Pont de Nemours, 750 F.2d 1569, 1574, 224 U.S.P.Q. 409, 411 (Fed. Cir. 1984).

Nonetheless, Applicant has amended the claims to recite that the recited intestinal damage comprises a morphological damage. The cited reference is clearly and absolutely silent with regard to treating, ameliorating, preventing, or protecting from intestinal damage that comprises, for example, morphological damage. Thus, for the reasons previously made of record, which are herein incorporated by reference in their entirety, as well as the foregoing, Applicant submits that cited prior art fails to disclose each and every element of the present claims, and therefore does not anticipate the instant claims.

Rejection under 35 U.S.C. § 103(a)

The Examiner has again rejected claim 14 under 35 U.S.C. § 103(a) as being allegedly unpatentable over Balasubramaniam (U.S. Patent No. 5, 604, 203), hereinafter '203, as applied to claims 1, 2, 5, and 10-12 above, and further in view of Dumont et al. 26:320-324 (1994). Specifically, the Examiner asserts that whereas '203 allegedly teaches a method of treating intestinal damage comprising administering a pharmaceutically active formulation of PYY or a PYY agonist to a human as applied to claims 1, 2, 5, and 10-12 above, '203 fails to teach the method of claim 14, comprising administering PYY[3-36]. The Examiner applies Dumont et al. in an attempt to cure the deficiencies of '203. Applicant respectfully traverses.

For the reasons provided above, at least, '203 fails to teach a method of treating intestinal damage that might result from a gastrointestinal disorder, per se, comprising administering a pharmaceutically active formulation of PYY or a PYY agonist polypeptide as instantly claimed. That Dumont et al. may teach that a PYY agonist, PYY[3-36], binds PYY receptors, as the Examiner contends, fails to cure the deficiencies of '203. Similar to that mentioned above, no nexus is provided linking alleged binding to PYY receptors to a method of treating intestinal damage per se, or in treating intestinal damage associated with the a condition or disorder, comprising administering a PYY or a PYY agonist polypeptide to treat the intestinal damage, as instantly claimed.

The Examiner has also again rejected claim 1-3, 5, 10, and 13 under U.S.C. § 103(a) as being allegedly unpatentable over El-Salhy et al (Peptides 23:397-402, February 2002). Specifically, the Examiner repeats the assertion that El-Salhy et al. teaches the following: "a decreased level of PYY in human patients with gastrointestinal disorders, including

inflammatory bowel diseases (examples as Crohn's disease and ulcerative colitis; pages 398-399)"; that "changes in PYY in gastrointestinal disorders could be beneficial in clinical practice and in cases where PYY increase is desirable, diet that increases PYY synthesis and release can be followed, or a receptor agonist can be utilized (Abstract; page 401)"; that "infusion of PYY in dogs increases colonic absorption of water, Na, and Cl ions, and PYY or its analogue can be of use as clinical agents in intestinal malabsorption disorders or after bowel resection". While the Examiner acknowledges that the reference "do[es] not explicitly teach the instantly claimed method," the Examiner concludes that it would nonetheless "have been obvious to one having ordinary skill in the art at the time the invention was made to administer to a subject or a human patient after bowel resection or to treat a gastrointestinal disorders (sic), including inflammatory bowel diseases (such a ulcerative colitis) (sic) with a reasonable expectation of success." The Examiner continues, contending that "[t]he administering PYY to a subject or a human patient with a gastrointestinal disorder would necessarily treat damage caused by the gastrointestinal disorder". Applicants traverse.

Applicant first notes that the allegation that "[t]he administering PYY to a subject or a human patient with a gastrointestinal disorder would necessarily treat damage caused by the gastrointestinal disorder" appears to inject an allegation of inherency into the Examiner's 103(a) obviousness rejection. It is clearly established that such allegations of inherency have no place in an obviousness-type rejection, and, in fact, may indicate non-obviousness:

> [T]he inherency of an advantage and its obviousness are entirely different questions. That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown. In re Shetty, 566 F.2d 81, 86, 195 U.S.P.Q. 753, 756-57 (C.C.P.A 1977)(quoting In re Spormann, 363 F.2d 444, 448, 150 U.S.P.Q. 449, 452 (C.C.P.A. 1966)

Secondly, as mentioned in Applicant's previous response, the alleged teachings of the El-Salhy reference are so ambiguous and contradictory such that no reasonable expectation of success can be reasonably inferred from such "teachings" (from Applicant's response filed December 19, 2007):

> the reference opines that certain "changes in PYY seem to be an adaptive response to certain such disorders", whereas in other disorders, such changes in PYY "appear to be primary and could be one of the etiologic factors of [such] disease[s]" (Abstract).

> Further, whereas "the concentration of PYY in tissue extracts …of patients with Crohn's colitis and ulcerative colitis has been found to be lower than in controls (paragraph bridging pages 398 and 399)", "basal and postprandial plasma levels of PYY in these patients are elevated in patients (sic) with celiac disease" (page 399, second paragraph). Further still, whereas in one study performed in the author's laboratory "PYY cells have been found to be increased as compared to controls in the ascending colon of patients with CST [chronic idiopathic slow transit constipation]," another study performed in the same laboratory determined that "the number of colonic PYY cells has not been found to be affected," and whereas "the concentration of PYY in colonic tissue extracts from patients with CST has been reported to be high, basal and peak plasma PYY levels have been reported to be unaffected" (page 399, last paragraph).
> The confused nature of the report is perhaps most epitomized by its conclusion:
>
> > The changes in PYY could be favorable in some intestinal disorders…[o]n the other hand, it could be harmful. The accumulated data of the changes in PYY in gastrointestinal disorders could be beneficial in clinical practice. Thus, in cases where PYY increase or decrease is desirable, diet that increases of decreases PYY synthesis and release can be used, or a receptor agonist or antagonist can be utilized. (page 402, last paragraph)

The Examiner's patent dismissal of the foregoing, and reliance of certain citations culled from the reference simply for the purpose of shoring up his 103(a) rejection is unavailing and improper:

> It is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the art.
> Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, 796 F.2d 443, 448(Fed. Cir. 1986), cert. denied, 484 U.S. 823 (1987) (quoting In re Wesslau, 353 F.2d 238, 241 (C.C.P.A. 1965)).

Nonetheless, Applicant has amended the claims to recite that the recited intestinal damage comprises a morphological damage. The cited references, singly, or when combined, are clearly and absolutely silent with regard to treating, ameliorating, preventing, or protecting from intestinal

damage that comprises, for example, morphological damage. Accordingly, for the foregoing reasons, at least, the Section 103(a) rejections are in error and should be withdrawn.

Conclusion

In conclusion, all rejections and objections outlined in the outstanding Office Action are in error and should be withdrawn.

Applicants believe that all issues raised in the Office Action have been properly addressed in this response and in the amendments to the claims as shown in the attached Listing of Claims. Accordingly, reconsideration and allowance of the amended claims is respectfully requested. If the Examiner feels that a telephone interview would serve to facilitate resolution of any outstanding issues, the examiner is encouraged to contact Applicants' representative at the telephone number below.

No additional fees are believed due for this submission. However, if a fee is due, the Commissioner is hereby authorized to charge payment of any fees associated with this communication, to Applicant's Deposit Account No. 010535 referencing Docket No. 0402US-UTL. Additionally, the Commissioner is hereby authorized to charge payment or credit overpayment of any fees during the pendency of this application to Applicant's Deposit Account No. 010535.

Date: November 7, 2008

Respectfully submitted,

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